

REMARKS

Entry of the foregoing amendments is respectfully requested.

Summary of Amendments

Upon entry of the foregoing amendments, claims 19, 26-36, and 38 are canceled, claims 17, 20, and 37 are amended, whereby claims 17, 20-25, 37, and 39 will be pending, with claims 17 and 37 being independent claims. Support for the amendments to the claims can be found in the specification, including the original claims.

Applicants emphasize that the amendment to the claims is without prejudice or disclaimer, and Applicants expressly reserve the right to prosecute the claims in their unamended form in one or more continuation and/or divisional applications.

Summary of Office Action

As an initial matter, Applicants note with appreciation that the Examiner has withdrawn the rejections under 35 U.S.C. § 35 U.S.C. § 112, first paragraph, set forth in the previous Office Action.

The Office Action indicates that claims 17, 19-30, and 33-39 are pending and under consideration. The Action rejects claims 19, 20, 33-36, and 38 under 35 U.S.C. § 112, first paragraph, claims 26-29 under 35 U.S.C. § 102(e), and claims 17, 19-30, and 33-39 under 35 U.S.C. § 103(a).

Response to Office Action

Withdrawal of the rejections of record is respectfully requested, in view of the foregoing amendments and the following remarks.

Response to Rejection of Claims under 35 U.S.C. § 112, First Paragraph

The Action rejects 19, 20, 33-36, and 38 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirements. In response, and without acquiescing to or agreeing with the rejection, Applicants respectfully note that independent claims 17 and 37 are amended and claims 19, 26-36, and 38 are canceled in the present Amendment. Applicants respectfully submit that the rejection under 35 U.S.C. § 112, first paragraph, is moot in view of the present amendments, and respectfully request withdrawal of the rejection.

Response to Rejection of Claims under 35 U.S.C. § 102(e)

The Office Action rejects claims 26-29 under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 6,491,943 to Tsuji et al. In response, and without acquiescing to or agreeing with the rejection, Applicants respectfully note that claims 26-29 have been canceled in the present Amendment. Applicants respectfully submit that the rejection under 35 U.S.C. § 102(e) is moot in view of the present amendments, and respectfully request withdrawal of the rejection.

Response to Rejection of Claims under 35 U.S.C. § 103(a)

The Office Action rejects claims 17, 19-30, and 33-39 under 35 U.S.C. § 103(a) as allegedly being unpatentable over HAMAGUCHI, in view of TSUJI. The rejection asserts that HAMAGUCHI teaches the use of a benzimidazole compound, i.e., TU-572, for the treatment of allergies such as anaphylaxis and urticaria via a reduction of IgE. TSUJI is alleged to teach that catechins suppress histamine release and can also treat allergies via a reduction of IgE, wherefore there would allegedly have been motivation to combine HAMAGUCHI with TSUJI.

Applicants note that HAMAGUCHI, while describing a single benzimidazole derivative, i.e., TU-572, which may be useful in the treatment of allergic diseases such as anaphylaxis and urticaria, clearly teaches that the effect of TU-572 is based on a mechanism, i.e., specific inhibition of CD45 (PTPase), which is completely different from the effect on which the present claims are based, i.e., inhibition of the secretion of IgE-dependent HRF by benzimidazole compounds with proton pump inhibitor activity.

HAMAGUCHI does not contain any indication that TU-572 exhibits proton pump inhibitor activity, nor does HAMAGUCHI teach or suggest that any benzimidazole compounds different from TU-572 have an activity similar to that of the latter. On the contrary, on page 320, middle of left column, of HAMAGUCHI, it is indicated that several benzimidazole derivatives were synthesized, but only TU-572 exhibited potent and specific inhibitory effects with respect to CD45.

Accordingly, even if one were to disregard the difference in the mechanism of action between TU-572 and the compounds recited in the present claims, HAMAGUCHI does not teach or suggest that any benzimidazole derivative different from TU-572 shows beneficial effects

with respect to the treatment of allergies such as anaphylaxis and urticaria. TSUJI does not cure the deficiencies of HAMAGUCHI in that it does not even relate to benzimidazole derivatives.

Specifically, HAMAGUCHI teaches that TU-572 exhibits an anti-allergic effect because it inhibits *tyrosine PTPase (Protein-Tyrosine-Phosphatase)*. Neither HAMAGUCHI nor any other documents published up to the present that Applicants are aware of teach or suggest that TU-572 has proton pump inhibitor activity. Further, Applicants are not aware that CD45 inhibition or similar physiological effects have ever been reported for compounds such as omeprazole and any of the other benzimidazole proton pump inhibitors recited in the present claims.

HAMAGUCHI performed experiments based on the theory that "*inhibition of CD45*" plays an important role in the anti-allergic effect. HAMAGUCHI found TU-572 through a high-throughput screening system in the course of a search for a compound having CD45 inhibitory activity, which compound happened to be a benzimidazole compound. In comparison, Applicants found that certain benzimidazoles having proton pump inhibitor activity such as, e.g., omeprazole, significantly reduce the release of HRF in the course of a search for compounds which can "*prevent the release of IgE-dependent HRF*". This further illustrates the fact that HAMAGUCHI has nothing to do with the present invention and is unable to teach or suggest the same.

According to TSUJI, the histamine-release inhibitory effect of catechin is because of its inhibitory effect on the influx of calcium ions into cells or the *phosphorylation of the tyrosine residue* of certain proteins which play an important role in the histamine release process, i.e., not because catechin exhibits proton pump inhibitory activity. Accordingly, the disclosure of TSUJI

that certain green tea catechins suppress histamine release and can treat allergies has nothing to do with the present invention.

Also, TSUJI fails to describe the precise histamine inhibitory mechanism of catechin. Further, the significant structural difference between catechins and benzimidazoles would have been another disincentive for one of ordinary skill in the art to combine HAMAGUCHI and TSUJI.

IgE-dependent histamine releasing factor (HRF) secreted from the immune cells such as macrophages binds with receptors on the cells like basophils and stimulates secretion of histamine, IL-3, IL-13, etc. which cause an immune response. Accordingly, the benzimidazoles having proton pump inhibitor activity used in the methods of the present invention inhibit the secretion of HRF and thereby indirectly, i.e., as a result of the inhibition of the secretion of HRF, also inhibit the secretion of histamine, IL-3, IL-13, etc. and eventually exhibit an anti-allergic effect. In comparison, both TU-572 and catechin are reported to directly inhibit the secretion of histamine (i.e. not via the inhibition of the secretion of HRF), which appears to be related to the phosphorylation of tyrosine (i.e., not to the secretion of HRF). That is, the compounds of the present invention can block an allergic reaction at an earlier stage than TU-572 and catechin can, which makes the method of the present invention more potent and efficient.

To sum up, considering the fact that the anti-allergic effect of TU-572 or catechin is due to reasons different from the inhibition of the secretion of HRF and that the inhibition of the secretion of HRF by proton pump inhibitors such as, e.g., omeprazole is neither taught nor suggested by the cited documents (and the prior art that Applicants are aware of in general),

HAMAGUCHI and TSUJI, alone or in combination, are unable to render obvious the subject matter of any of the claims submitted herewith.

In view of the foregoing remarks and amendments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 17, 20-25, 37, and 39 under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing, it is believed that all of the claims in this application are in condition for allowance, which action is respectfully requested. If any issues yet remain which can be resolved by a telephone conference, the Examiner is respectfully invited to contact the undersigned at the telephone number below.

Respectfully Submitted,
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